PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
PF-0714 PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US 00/ 19698	19/07/2000	19/07/1999
Applicant		
INCYTE GENOMICS, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 7 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   ☒ contained in the international application in written form.

   ☒ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readble form.

   ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   ☐ the text is approved as submitted by the applicant.

   ☒ the text has been established by this Authority to read as follows:

   GTP-BINDING PROTEIN ASSOCIATED FACTORS

5. With regard to the **abstract,**

   ☒ the text is approved as submitted by the applicant.

   ☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   ☐ as suggested by the applicant.

   ☐ because the applicant failed to suggest a figure.

   ☐ because this figure better characterizes the invention.

   ☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/19698

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 18, 21 and 24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-28 all partially

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-28, all partially

A protein with at least 90% identity to seq.ID.1 or biologically active or immunogenic fragment thereof, polynucleotide encoding it, optionally transcriptionally linked to a promoter, cell transformed therewith, transgenic organism comprising said polynucleotide, method for producing said protein using said cell, antibody against said protein, polynucleotides having at least 70% sequence homology to seq.ID.67 of at least 60 nt, method for detecting said nucleic acid by hybridization with a probe of at least 20 nt or by amplification, pharmaceutical composition of the protein, methods for screening for (ant)agonists of the protein or modulators of the proteins expression or activity and compounds identified thereby.

Inventions 2-61: claims 1-28, all partially

Subject matter as defined above under invention 1, but limited to the respective protein/nucleic acid sequences:

2. 2 and 68,
3. 3 and 69,
4. 4 and 70,
5. 5 and 71,
6. 6 and 72,
7. 7 and 73,
8. 8 and 74,
9. 9 and 75,
10. 10 and 76,
11. 11 and 77,
12. 12 and 78,
13. 13 and 79,
14. 14 and 80,
15. 15 and 81,
16. 16 and 82,
17. 17 and 83,
18. 18 and 84,
19. 19 and 85,
20. 20 and 86,
21. 21 and 87,
22. 22 and 88,
23. 24 and 90,
24. 25 and 91,
25. 26 and 92,
26. 27 and 93,
27. 29 and 95,
28. 30 and 96,
29. 31 and 97,
30. 32 and 98,
31. 33 and 99,
32. 34 and 100,

Continuation of Box I.2

Claim 12 of the underlying application relates to a polynucleotide comprising at least 60 nt of a polynucleotide, which has at least 70% sequence identity to a nucleic acid sequence selected from those listed in claim 5. Since the at least 60 nucleotides need not originate from an area of homology with any of the sequences of claim 5, the polynucleotide claimed in claim 12 is not defined in any way. The search of said claim has been limited to nucleic acids comprising a nucleic acid sequence having at least 70% homology to a nucleic acid sequence selected from claim 5 of at least 60 nt in length.

Present claims 20 and 23 refer to agonists and antagonists, respectively, defined by reference to a desirable characteristic or property, namely the fact that they can be obtained by certain screening methods. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to proteins with at least 90% homology to seq.ID.1 and antibodies thereto.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

33.36 and 102,
34.37 and 103,
35.38 and 104,
36.39 and 105,
37.40 and 106,
38.41 and 107,
39.43 and 109,
40.44 and 110,
41.45 and 111,
42.46 and 112,
43.47 and 113,
44.48 and 114,
45.49 and 115,
46.50 and 116,
47.52 and 118,
48.53 and 119,
49.54 and 120,
50.55 and 121,
51.56 and 122,
52.57 and 123,
53.58 and 124,
54.59 and 125,
55.60 and 126,
56.61 and 127,
57.62 and 128,
58.63 and 129,
59.64 and 130,
60.65 and 131, and
61.66 and 132.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/19698

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C07K14/47 G01N33/53 C12Q1/68 A61K38/17
C07K16/18 A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K G01N C12Q A61K A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMEST_HUM1 [Online] Entry/Acc.no. AA679577, 4 December 1997 (1997-12-04) HILLIER, L. ET AL.: "zj49c09.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 453616 3' similar to TR:G1230663 G1230663 SIMILAR TO E. COLI HYPOTHETICAL 22.1 KD PROTEIN IN POLA 3' REGION." XP002148938 the whole document --- -/--	11-15

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
2 October 2000	08.01.01

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Smalt, R

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL - EMEST_HUM13 [Online] Entry HS1229641, Acc.no. AA429983, 25 May 1997 (1997-05-25) HILLIER, L. ET AL.: "zw60f01.r1 Soares_total_fetus_Nb2HF8_9w Homo sapiens cDNA clone IMAGE:774457 5' similar to SW:YSXC_BACSU P38424 HYPOTHETICAL 22.0 KD PROTEIN IN LON-HEMA INTERGENIC REGION ;, mRNA sequence." XP002148939 the whole document	11-15

A	DATABASE EMBL - EMEST_ROD2 [Online] Entry/Acc.no. AI122094, 8 September 1998 (1998-09-08) MARRA, M. ET AL.: "uc46f10.r1 Soares mouse mammary gland NMLMG Mus musculus cDNA clone IMAGE:1401067 5' similar to SW:Y335_MYCGE P47577 HYPOTHETICAL GTP-BINDING PROTEIN MG335. ;, mRNA sequence." XP002148940 the whole document	

P,X	DATABASE EMBL - EMHUM2 [Online] Entry/Acc.no. AF161484, 1 February 2000 (2000-02-01) YE, M. ET AL.: "Homo sapiens HSPC135 mRNA, complete cds." XP002148941 the whole document	1,3,6-9, 11-16, 20,23

P,X	WO 99 58675 A (CHIRON CORP ;HYSEQ INC (US)) 18 November 1999 (1999-11-18) the whole document	11-15

A	CLAPHAM, D.E. ET AL.: "New roles for G-protein beta-gamma-dimers in transmembrane signalling." NATURE, vol. 365, 30 September 1993 (1993-09-30), pages 403-6, XP002148967 cited in the application the whole document	

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/19698

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9958675 A	18-11-1999	AU 4187499 A	29-11-1999
		AU 2095599 A	19-07-1999
		EP 1053319 A	22-11-2000
		WO 9933982 A	08-07-1999
		WO 9938972 A	05-08-1999
		AU 6263999 A	17-04-2000
		WO 0018916 A	06-04-2000

10/031660

PATENT COOPERATION TREATY

RECD 22 MAY 2002

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PF-0714 PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/19698	International filing date *(day/month/year)* 19 July 2000 (19.07.2000)	Priority date *(day/month/year)* 19 July 1999 (19.07.1999)

International Patent Classification (IPC) or national classification and IPC

IPC(7): C12N 1/10, 1/13, 1/15, 1/21, 5/1015/12; C12Q 1/68; C07K 14/435 and US Cl.: 530/350; 536/23.5; 435/6, 69.1, 325, 410, 252.3, 254.11

Applicant

INCYTE GENOMICS, INC.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 62 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
- IV ☒ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14 February 2001 (14.02.2001)	02 May 2002 (02.05.2002)
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer John S. Brusca Telephone No. 703 308-0196

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/19698

I. Basis of the report

1. With regard to the **elements** of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-110 as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the claims:
pages 111-117 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☐ the drawings:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-115 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- ☒ restricted the claims.
- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is

- ☐ complied with.
- ☒ not complied with for the following reasons:

Please See Continuation Sheet

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- ☐ all parts.
- ☒ the parts relating to claims Nos. 1-7, 9, and 11-15 and SEQ ID NOS: 1 and 67

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	1-7, 9	YES
	Claims	11-15	NO
Inventive Step (IS)	Claims	1-7, 9	YES
	Claims	11-15	NO
Industrial Applicability (IA)	Claims	NONE	YES
	Claims	1-7, 9, 11-15	NO

2. CITATIONS AND EXPLANATIONS

Claims 11-15 lack novelty under PCT Article 33(2) as being anticipated by Hillier et al. (GenBank Accession No. AA679577.

Claims 11-15 lack novelty under PCT Article 33(2) as being anticipated by Hillier et al. (GenBank Accession No. AA429983).

Claims 11-15 lack novelty as being anticipated by the two Hillier et al. references cited above. This determination is based on the results of the EPO search report. It is noted that the International Examination Authority does not have a computer readable form of the sequence listing, so a nucleotide or amino acid sequence alignment was not possible.

Claims 1-7, 9, and 11-15 lack industrial applicability as defined by PCT Article 33(4).

The claimed nucleic acid and protein compounds lack industrial applicability because the disclosed uses of the nucleic acids and proteins are not specific and are generally applicable to any nucleic acid and protein. The description states that the nucleic acid compounds may be useful as probes for assisting in the isolation of full-length cDNAs or genes which would be used to make protein and optionally further usage to make the corresponding antibodies, gene mapping, isolation of homologous sequences, detection of gene expression such as in Northern blot analysis, molecular weight markers, chromosomal markers, and for numerous other generic genetic engineering uses. Similarly, protein may be used for detection of expression, antibody production, Western blots, etc. These are non-specific uses that are applicable to nucleic acids and proteins in general and not particular or specific to the nucleic acids and proteins being claimed.

Further, the claimed nucleic acid and protein compounds lack industrial applicability because no practical application has been established for the claimed subject matter. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function lacks a currently available industrial application. A starting material that can only be used to produce a final product does not have industrial applicability in those instances where the final product lacks industrial applicability. In this case, none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acids have industrial applicability. The research contemplated by the applicants to characterize potential protein products, especially their biological activities, does not constitute an industrial applicability. The disclosure as filed does not suggest any property or activity for the nucleic acid and protein compounds such that another non-asserted industrial application would be well established for the compounds.

Claims 1-7 and 9 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the recited polynucleotides or polypeptides.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

IV. 3. This Authority considers that the requirement of unity of invention is accordance with Rules 13.1, 13.2 and 13.3 is not complied with for the following reasons:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-7, 9, and 11-15, drawn to a first set of related products consisting of a polynucleotide and a polypeptide encoded by the polynucleotide, cells comprising the polynucleotide, a first method of making the polypeptide, and a first method of using the polynucleotide as a probe.

Group II, claim(s) 8, drawn to a second product consisting of transgenic animals comprising the polynucleotide of Group I.

Group III, claim(s) 10, drawn to a third product consisting of antibodies specific to the polypeptide of Group I.

Group IV, claim(s) 16 and 17, drawn to a fourth product consisting of a pharmaceutical comprising the polypeptide of Group I.

Group V, claim(s) 18, drawn to a second method of use consisting of a therapeutic method of use of the polypeptide of Group I.

Group VI, claim(s) 26, 19, and 22, drawn to a third method of use consisting of a method of screening of modulators of activity of the polypeptide of Group I.

Group VII, claim(s) 20 and 23, drawn to a fifth product consisting of modulators of activity of the polypeptide of Group I.

Group VIII, claim(s) 21 and 24, drawn to a fourth method of use consisting of a therapeutic method of use of modulators of the polypeptide of Group I.

Group IX, claim(s) 25, drawn to a fifth method of use consisting of a method of screening of a ligand of the polypeptide of Group I.

Group X, claim(s) 27, drawn to a sixth method of use consisting of a method of screening for a modulator of expression of the polypeptide of Group I.

Group XI, claim(s) 28, drawn to a seventh method of use consisting of a method of assessing toxicity of a compound by measurement of hybridization between a biological sample treated with said compound and the polynucleotide of Group I.

In addition, each Group detailed above reads on distinct Groups drawn to multiple pairs of polynucleotide and polypeptide sequences encoded by the polynucleotides. The pairs of sequences are distinct because they are unrelated sequences and a further lack of unity is applied to each Group detailed above. The applicants must elect a single pair of sequences for examination for any elected Group detailed above. Payment of fees for an additional invention will entitle the applicants to one combination of a single pair of sequences and a single additional Group detailed above.

The total number of inventions was calculated based on the numbers that exist between the pairs of SEQ ID NOS and the total number of Groups. The formula is recited below:
Total number of inventions = (Total Groups + additional species in the groups) X Total pairs of sequences
This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

For Group VI the first species is a method of screening for agonists of activity of the polypeptide of Group I, and the second species is a method of screening for antagonists of activity of the polypeptide of Group I.

For Group VII, the first species is an agonist of activity of the polypeptide of Group I, and the second species is an antagonist of activity of the polypeptide of Group I.

For Group VIII, the first species is a therapeutic method of using agonists of activity of the polypeptide of Group I, and the second species is a therapeutic method of using antagonists of activity of the polypeptide of Group I.

The claims are deemed to correspond to the species listed above in the following manner:

Group VI agonist: claim 19
Group VI antagonist: claim 22
Group VII agonist: claim 20
Group VII antagonist: claim 23
Group VIII agonist: claim 21
Group VIII antagonist: claim 24

The following claim(s) are generic: Group VI: claim 26.

The inventions listed as Groups I-XI, the species detailed above, and the 66 claimed pairs of sequences do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: PCT Rule 13.1 and Annex B do not provide for unity of invention between two or more different products, methods of making, or methods of use that share a special technical feature.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 January 2001 (25.01.2001)

PCT

(10) International Publication Number
WO 01/05970 A2

(51) International Patent Classification[7]: C12N 15/12, C07K 14/47, G01N 33/53, C12Q 1/68, A61K 38/17, C07K 16/18, A01K 67/027

(21) International Application Number: PCT/US00/19698

(22) International Filing Date: 19 July 2000 (19.07.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/144,595	19 July 1999 (19.07.1999)	US
60/150,460	23 August 1999 (23.08.1999)	US
60/159,849	15 October 1999 (15.10.1999)	US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier applications:

US	60/144,595 (CIP)
Filed on	19 July 1999 (19.07.1999)
US	60/150,460 (CIP)
Filed on	23 August 1999 (23.08.1999)
US	60/159,849 (CIP)
Filed on	15 October 1999 (15.10.1999)

(71) Applicant *(for all designated States except US)*: **INCYTE GENOMICS, INC.** [US/US]; 3160 Porter Drive, Palo Alto, CA 94304 (US).

(72) Inventors; and

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(74) Agents: **HAMLET-COX, Diana** et al.; Incyte Genomics, Inc., 3160 Porter Drive, Palo Alto, CA 94304 (US).

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Published:

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/05970 A2

(54) Title: GTP-BINDING ASSOCIATED PROTEINS

(57) Abstract: The invention provides human GTP-binding associated proteins (GBAP) and polynucleotides which identify and encode GBAP. The invention also provides expression vectors, host cells, antibodies, agonists, and antagonists. The invention also provides methods for diagnosing, treating, or preventing disorders associated with expression of GBAP.

INTERNATIONAL SEARCH REPORT

Inter[redacted]Application No
PCT/US 00/19698

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12N15/12 C07K14/47 G01N33/53 C12Q1/68 A61K38/17
C07K16/18 A01K67/027

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12N C07K G01N C12Q A61K A01K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMEST_HUM1 [Online] Entry/Acc.no. AA679577, 4 December 1997 (1997-12-04) HILLIER, L. ET AL.: "zj49c09.s1 Soares fetal liver spleen 1NFLS S1 Homo sapiens cDNA clone 453616 3' similar to TR:G1230663 G1230663 SIMILAR TO E. COLI HYPOTHETICAL 22.1 KD PROTEIN IN POLA 3' REGION." XP002148938 the whole document --- -/--	11-15

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
2 October 2000	08.01.01

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Smalt, R

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE EMBL - EMEST_HUM13 [Online] Entry HS1229641, Acc.no. AA429983, 25 May 1997 (1997-05-25) HILLIER, L. ET AL.: "zw60f01.r1 Soares_total_fetus_Nb2HF8_9w Homo sapiens cDNA clone IMAGE:774457 5' similar to SW:YSXC_BACSU P38424 HYPOTHETICAL 22.0 KD PROTEIN IN LON-HEMA INTERGENIC REGION ;, mRNA sequence." XP002148939 the whole document	11-15

A	DATABASE EMBL - EMEST_ROD2 [Online] Entry/Acc.no. AI122094, 8 September 1998 (1998-09-08) MARRA, M. ET AL.: "uc46f10.r1 Soares mouse mammary gland NMLMG Mus musculus cDNA clone IMAGE:1401067 5' similar to SW:Y335_MYCGE P47577 HYPOTHETICAL GTP-BINDING PROTEIN MG335. ;, mRNA sequence." XP002148940 the whole document	

P,X	DATABASE EMBL - EMHUM2 [Online] Entry/Acc.no. AF161484, 1 February 2000 (2000-02-01) YE, M. ET AL.: "Homo sapiens HSPC135 mRNA, complete cds." XP002148941 the whole document	1,3,6-9, 11-16, 20,23

P,X	WO 99 58675 A (CHIRON CORP ;HYSEQ INC (US)) 18 November 1999 (1999-11-18) the whole document	11-15

A	CLAPHAM, D.E. ET AL.: "New roles for G-protein beta-gamma-dimers in transmembrane signalling." NATURE, vol. 365, 30 September 1993 (1993-09-30), pages 403-6, XP002148967 cited in the application the whole document	

INTERNATIONAL SEARCH REPORT

Ir ational application No.
PCT/US 00/19698

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 18, 21 and 24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: -
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-28 all partially

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-28, all partially

A protein with at least 90% identity to seq.ID.1 or biologically active or immunogenic fragment thereof, polynucleotide encoding it, optionally transcriptionally linked to a promoter, cell transformed therewith, transgenic organism comprising said polynucleotide, method for producing said protein using said cell, antibody against said protein, polynucleotides having at least 70% sequence homology to seq.ID.67 of at least 60 nt, method for detecting said nucleic acid by hybridization with a probe of at least 20 nt or by amplification, pharmaceutical composition of the protein, methods for screening for (ant)agonists of the protein or modulators of the proteins expression or activity and compounds identified thereby.

Inventions 2-61: claims 1-28, all partially

Subject matter as defined above under invention 1, but limited to the respective protein/nucleic acid sequences:

2. 2 and 68,
3. 3 and 69,
4. 4 and 70,
5. 5 and 71,
6. 6 and 72,
7. 7 and 73,
8. 8 and 74,
9. 9 and 75,
10. 10 and 76,
11. 11 and 77,
12. 12 and 78,
13. 13 and 79,
14. 14 and 80,
15. 15 and 81,
16. 16 and 82,
17. 17 and 83,
18. 18 and 84,
19. 19 and 85,
20. 20 and 86,
21. 21 and 87,
22. 22 and 88,
23. 24 and 90,
24. 25 and 91,
25. 26 and 92,
26. 27 and 93,
27. 29 and 95,
28. 30 and 96,
29. 31 and 97,
30. 32 and 98,
31. 33 and 99,
32. 34 and 100,

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

33.36 and 102,
34.37 and 103,
35.38 and 104,
36.39 and 105,
37.40 and 106,
38.41 and 107,
39.43 and 109,
40.44 and 110,
41.45 and 111,
42.46 and 112,
43.47 and 113,
44.48 and 114,
45.49 and 115,
46.50 and 116,
47.52 and 118,
48.53 and 119,
49.54 and 120,
50.55 and 121,
51.56 and 122,
52.57 and 123,
53.58 and 124,
54.59 and 125,
55.60 and 126,
56.61 and 127,
57.62 and 128,
58.63 and 129,
59.64 and 130,
60.65 and 131, and
61.66 and 132.

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claim 12 of the underlying application relates to a polynucleotide comprising at least 60 nt of a polynucleotide, which has at least 70% sequence identity to a nucleic acid sequence selected from those listed in claim 5. Since the at least 60 nucleotides need not originate from an area of homology with any of the sequences of claim 5, the polynucleotide claimed in claim 12 is not defined in any way. The search of said claim has been limited to nucleic acids comprising a nucleic acid sequence having at least 70% homology to a nucleic acid sequence selected from claim 5 of at least 60 nt in length.

Present claims 20 and 23 refer to agonists and antagonists, respectively, defined by reference to a desirable characteristic or property, namely the fact that they can be obtained by certain screening methods. The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to proteins with at least 90% homology to seq.ID.1 and antibodies thereto.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

...ormation on patent family members

Interr[illegible]pplication No
PCT/US 00/19698

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9958675 A	18-11-1999	AU 4187499 A	29-11-1999
		AU 2095599 A	19-07-1999
		EP 1053319 A	22-11-2000
		WO 9933982 A	08-07-1999
		WO 9938972 A	05-08-1999
		AU 6263999 A	17-04-2000
		WO 0018916 A	06-04-2000

US 1003166007P1

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No.	Doccode	Number of pages
1	CRFL	6

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